REMARKS

The Office Action dated May 17, 2005 has been received and carefully studied.

The Examiner maintains the rejection of claims 7, 13-15 and 18-20 under 35 U.S.C. §112, first paragraph, as being non-enabling. The Examiner states that the specification does not enable the use of the compounds to treat or prevent the diseases recited.

In order to expedite allowance, by the accompanying amendment claim 7 has been amended to recite "dermal disorders, bronchial and pulmonary disorders and gastroenterological disorders", since such language has express support in the specification. Although Applicants continue to disagree that the current language is not found in the specification, as it need not be found *ipsis verbis*, the amendment is being made to expedite allowance. Amendments to the claims that depend on claim 7 are made for consistency.

Furthermore, Applicants respectfully submit that the skilled artisan would be able to use the inventive compound to treat these disorders without undue experimentation. Indeed, the specification teaches that the inventive compound may be used for various therapeutic indications, including such indications for which ketotifen may be useful (but avoiding the severe dose-limiting sedative side effects of ketotifen). This statement alone provides sufficient guidance to the skilled artisan and would not require undue experimentation to implement. Applicants

respectfully submit that the skilled artisan would have a strong expectation that administration of this compound (administration of a compound with the pharmacological properties that have now been found for S-norketotifen), would be effective for treating the disorders recited.

The Examiner states that the language "S-isomer of a metabolite of ketotifen and having the structure . . ." is not found in the specification. Applicants respectfully disagree. The formula of claim 1 is expressly shown on page 2 of the PCT published application. The S-isomer of norketotifen is disclosed throughout the specification, including the synthesis mentioned at pages 5-6.

The Examiner states that the language "being substantially free of the corresponding R-isomer" is not found in the specification. Support for this language can be found in the various synthesis examples, where the isomeric purity of the resulting product is expressed as "ee". Thus, 95% ee of S-norketotifen is 95% of the S-isomer. This is clearly substantially free of the corresponding R-isomer.

The Examiner rejects claims 1, 7-10, 13-15, 18, 19 and 21 under 35 U.S.C. §112, second paragraph, as being indefinite. The Examiner considers the term "substantially" to be unclear. Applicants respectfully disagree, for the reasons stated above. This phrase "substantially free of its corresponding R-isomer is commonly used where optical isomerism is present, and in

conjunction with the "ee" values recited in the various synthetic examples, is clear to those skilled in the art.

With respect to whether some of the recited disorders are inflammatory disorders, Applicants have removed the term "inflammatory" to expedited allowance.

The Examiner rejects claims 1, 7-10, 13, 15, 18, 19, 21 under 35 U.S.C. §103(a) as being unpatentable over Aberg I, WO 98/56381 or Aberg II, WO 98/43640 in view of Polivka I or Polivka II.

The rejection is respectfully traversed.

Applicants respectfully but vigorously disagree with the Examiner's unsupported statement that because ketotifen is know to be optically active as shown by Polivka I and II, one of ordinary skill in the art would "expect" norketotifen to be optically active. This simply is not true. Polivka I and II are silent as to whether the compound norketotifen is chiral or non-chiral, and are silent as to whether norketotifen is a mixture of chemically stable atropisomers. Based upon the rare atropisomerism exhibited by ketotifen, and the presence of the methyl group on the piperidine nitrogen that is believed to lead to such atropisomerism, **and the absence of that methyl group** in the claimed compound, the expectation is that the claimed compound would not be optically active. Moreover, even if somehow one skilled in the art did have some expectation of optical activity in the claimed compound, it remains completely

unexpected that the claimed compound would be devoid of the severe sedative side effects of ketotifen.

The Examiner rejects claims 1 and 21 under the judicially created doctrine of obviousness-type double patenting over claim 7 of U.S. Patent No. 6,207,684 in view of Polivka I or II.

The rejection is respectfully traversed.

As stated above, one skilled in the art would have no expectation that norketotifen exhibits optical isomerism, and even if expectation were present, it is completely unexpected that the claimed compound would be devoid of the severe sedative side effects of ketotifen.

The allowance of claim 6 is noted with appreciation.

Reconsideration and allowance are respectfully requested in view of the foregoing.

Respectfully submitted,

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